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10/574,213

10/09/2006

Dirk Vetter

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EXAMINER

KOSAR, AARON J

ART UNIT

PAPER NUMBER

1651

MAIL DATE

DELIVERY MODE

10/07/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/574,213 | Applicant(s) VETTER ET AL. | |
| | Examiner AARON J. KOSAR | Art Unit 1651 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-62 is/are pending in the application.
- 4a) Of the above claim(s) 41,43-47,54-58,60 and 61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-40,42,48-53,59 and 62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/31/06;7/28/06;9/16/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

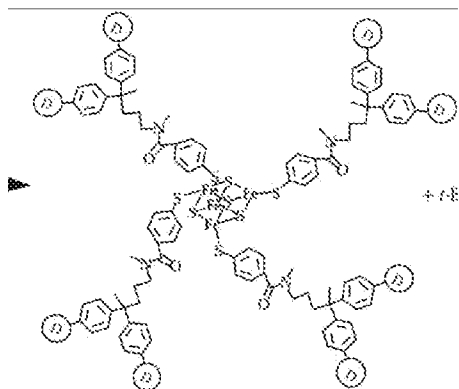
Election/Restrictions

Applicant's election of Group I and the species of compound (90), in the reply filed May 28, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The election/restriction requirement is still deemed proper and therefore made FINAL.

Claims 32-62 are pending of which claim 62 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The elected species (i.e. structure (90) having a defined Michael addition thio-succinimidyl bonding) has been examined on the merits and found free of the art.

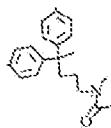
Accordingly, the search was expanded to include the following species (I*) which was selected by the Examiner for examination on the merits.



(I*).

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Species (I*) contains, for example, a hyperbranched polymer/dendrimer (D) having further



structure of (e.g. a core) and a $\text{Fe}_4\text{-S}_4$ cluster (e.g. a biologically active moiety) linked to



a structure (e.g. a linker). The selected species (I*) is drawn to claims 32-40, 42, 48-53, 59, and 62, and the species *N,O, amide, amino, and non-saturated cyclic groups*.

Accordingly, claims 41, 43-47, 54-58, and 60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

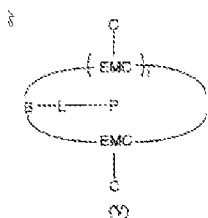
Claims 32-40, 42, 48-53, 59, and 62 have been examined on the merits.

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Specification

The disclosure is objected to because of the following informalities:

The chemical formula (V-VIII, XVII-XVIII, XXI and XXII), on pages 23, 24, 31, 34, and 35 are objected to because is it unclear if the converging lines (to the right side of each structure): (i) if each line has an intended atomic structure or bond not defined by EMC or C; (ii) if the intersection/convergence of the lines implies a bond; and (iii) how the elected structure of formula (90) corresponds to the elected formula (V), especially regarding the fragment thereof extending to the right of the "EMC" (see e.g. fig V, below).



Appropriate correction is required.

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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-40, 42, 48-53, 59, and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re *Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985)

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(quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See M.P.E.P. § 2163.02. In this case, the skilled artisan would not have reasonably concluded at the time of the invention that applicant was in possession of the entire invention as claimed.

In this case, Giehm *et al* (*Biopolymers*, 2008, 89(6), pp 522-529.), writing years after the instant filing, teach that skilled artisans had not elucidated the effects of the genus of dendrimers or the genus of all biologically active moieties or proteins (and linked derivatives thereof) having activity in the genus of dendrimers, or even identified all of the properties which would permit, *a priori*, selection of combinations which would be biologically active, except by trial-and-error (e.g. Giehm teaches that “protein-dendrimer interactions involve a mixed bag of specific and general interactions” and thus it is “difficult in general to predict whether a given protein will be destabilized or unaffected by dendrimers”, e.g. page 528, pgh.1). Furthermore, the effectors of biological activity were not identified even years after the instant invention as taught by Giehm which teach that insulin is destabilized (denatured/deactivated) by dendrimers (e.g. “3rd generation dendrimer is the most effective destabilizer and precipitator of insulin”, page 528, pgh.2). Given these teachings, the skilled artisan would not have reasonably concluded at the time of filing that applicants possessed the genus of all combinations of all hyperbranched polymers (dendrimers) and biologically active moieties and all structural combinations thereof.

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It is noted that the claims in no way limit the scope of the structure of the composition to a fully structural-defined chemical structure (e.g. the elected/disclosed structure). Claims 32-40, 42, 48-53, 59, and 62 refer to "hyperbranched polymer", a "core", and a "moiety" wherein the claims are not limited to any structure, and as discussed in the section 112, second paragraph, rejections below, this term(s) is/are not limited to any particular fully-disclosed or structurally-defined composition. The terms "polymer", "hyperbranched polymer", "core", and "moiety" encompasses any and all polymer-moiety compositions that share in some way a structural or functional similarity to some composition from any polymer-moiety combination.

The specification clearly and explicitly indicates, insulins may be utilized in the instant composition (e.g. page 22, line 6) although the composition of the instant claims are described only by the limited exemplified species and the specification provides no guidance (other than implied trial-and-error) for determining which " hyperbranched polymer", "core", "moiety", and the structurally-defined combinations thereof which would provide "biologically activity" in the composition and which would not; this level of disclosure is insufficient because the only means provided for finding such a compound having a biological activity is essentially a trial-and-error process.

Since there were no compounds known to have the required function, and in the instant application, the quantity of fully-defined compositions (or sufficient guidance and direction as to how one would select *a priori* a particular combination of polymer-linker-moiety) that would be reasonably expected to have biological activity are not adequately disclosed. The key relevant to this ground of rejection is the fact that no method (other than trial-and- error) is provided for

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identifying compounds having the desired biological activity (biologically active moiety). For this reason, the rejection due to lack of written description is proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32-40, 42, 48-53, 59, and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-40, 42, 48-53, 59, and 62 are indefinite because the claims recite a polymer-core-linker-moiety linkage; however, claim 32 does not recite any minimal structure and thus it is unclear what structure Applicant intends to minimally define each of “polymer”, “core”, moiety”, and “linker” and it is further unclear which of the components of the dependent claims are the same as or distinguished from the components of the preceding claims (e.g. it is unclear how one would determine from the claims whether a group is a branching center, branching group, (branched) molecular chain, and/or capping group . Clarification is required.

Claim 35 recites the terms "the polymer chains", “linear” (alkyl chain), “branched” (alkyl chain), and “cyclical alkyl chains”; however it is unclear how the terms are related structurally to “a hyperbranched polymer” and/or “core” and/or “biologically active moiety” of the claimed composition of claim 32. Clarification is required.

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Claim 35, 37, and 48 recite the limitations “polymer chains”, “molecular chains”, and “the encapsulating organic compound”, respectively. There is insufficient antecedent basis for these limitations in the claims. Clarification is required.

Claims 36, 39, 52, and 53 recites numerous parenthetical terms; however it is unclear (i) which terms are abbreviations, which parenthesis are merely to emphasize the abbreviations contained therein, and which hyphens are charges (⁻), bonds (“-”), or defining minimal units (e.g. “(-S-S)-” vs. -S-S-, ~~(S-S)~~ or ~~[S-S]~~ ; (-S-S-), (~~(S-S)~~), or (~~[S-S]~~), etc.). The claims are also unclear because the term “amide (-C(O)NR-)” includes R = H and is thus unclear what is intended by Applicant's separate recitation of “amide -C(O)NH- or -C(O)NR-“. Still further, it is unclear if “oxypropylene and oxybutylene” is a single species or multiple species (If the latter the terms should be comma-separated). Thus it is unclear which compounds and which terms are required by the claims and intended by Applicant and which are merely exemplary. Clarification is required.

Claim 37 recites the term “sterically demanding”; however, it is unclear what is intended by the term. If Applicant intends to recite “sterically-hindering”. Clarification is required.

The term “highly” in claim 40 is a relative term which renders the claim indefinite. The term “highly” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably

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apprised of the scope of the invention. Please note the phrase “with a branching degree of between 2 and 6” is unclear if the term is further limiting of the capping group or the centers and thus does not resolve this deficiency. Clarification is required.

Claim 50 recites “linkable linked”; however, it is unclear if the groups are linkable (unlinked) or if they are linked. Clarification is required.

All other claims depend directly or indirectly from the rejected claims and are, therefore, also rejected under 35 USC § 112, second paragraph, for the reasons set forth above.

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Claim Rejections - 35 USC § 102

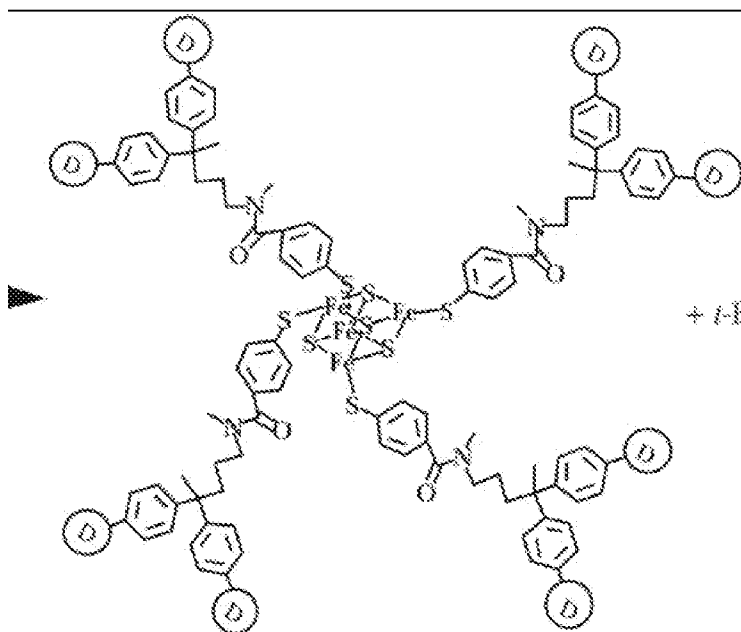
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32-40, 42, 48-53, 59, and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorman (*C.R.Cimie*, 6 (2003), pg. 911-918.).

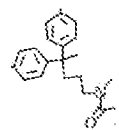
Gorman anticipates the claims by teaching the dendrimeric complex:



Inherent to the structure and or expressly recited by Gorman, is the complex comprising an iron-sulfur [Fe_4S_4] cluster (biologically active moiety/biopolymer), at the core of and S-linked (linker)

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to a dendrimeric polymer (D)(hyperbranched polymer with a core) (see whole document, e.g. pg 913, fig.1). The hyperbranched polymer/dendrimer (D) comprises a further structure of



(e.g. a core) linked to a structure



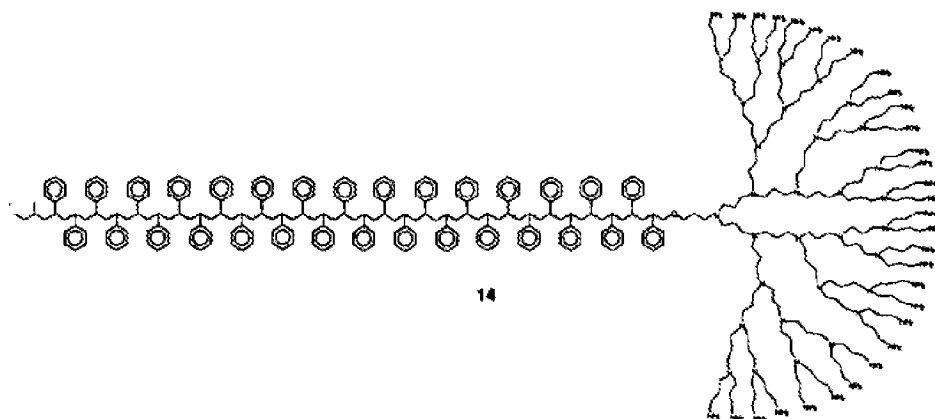
(e.g. a linker) and contains therein multiple N, O,

amide, amino, non-saturated cyclic groups, linear alkyl groups, branching centers, alkyl chains, and capping groups.

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Claim 32, 33, and 35-39, 48, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by van Hest *et al* (*Chem. Eur. J.* 1996, 2(12), 1616-1626.)

Van Hest anticipates the claims by teaching a composition comprising (a) a hyperbranched polymer; (b) a core; (c) a biologically active moiety; (d) a linker; (e) the polymer attached to the core; and (f) the moiety attached to the polymer via a linker. Specifically, van Hest teaches the composition of formula (14):



wherein the composition comprises (a) a dendrimeric composition (hyperbranched polymer) having (b) a central/core structure comprising (d) a linking $[\text{OCH}_2\text{CH}_2\text{CH}_2\text{N}]$ moiety and (c) amine ($-\text{RNH}_2$) (moieties, capping groups); wherein (e) the dendrimers are attached to the core structure and wherein the NH_2 moieties are linked to the core via the n^{th} -generation dendrimer. The structure further comprises water-solublizing amine groups along the periphery of the dendrimer, multiple molecular chains, including linear and branching chains; and N and S heteroatoms in the polymer chain.

Although Van Hest does not teach the elected/selected species, van Hest demonstrates the non-allowability of the generic invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. KOSAR whose telephone number is (571)270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Aaron J Kosar/
Examiner, Art Unit 1651

/Christopher R. Tate/
Primary Examiner, Art Unit 1655